Environmental Health
PERSPECTIVES
Journal of the National Institute of Environmental Health Sciences

ehponline.org

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doi:10.1289/ehp.5780 (available at http://dx.doi.org/)
Online 23 January 2003

The National Institute of Environmental Health Sciences
National Institutes of Health
Department of Health and Human Services

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* This paper represents the opinions of the authors and may not reflect the official positions and recommendations of the OECD.

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Running Title: OECD Uterotrophic Bioassay Validation – Dose Response Studies

Headers: Authors: Kanno et al.
Title: OECD Uterotrophic Bioassay Validation – Dose Response Studies

Key words: endocrine disruption, estrogen, rat uterus, uterotrophic.

Abbreviations used: Bisphenol A, BPA; Coefficient of variation, CV; 1,1,1-trichloro-2,2-bis(*o,p'*-chlorophenyl)methane, *o,p'*-DDT; Endocrine Disrupters Testing and Assessment, EDTA; Ethinyl estradiol, EE; Genistein, GN; Methoxychlor, MX; Lowest observed effect level, LOEL; Nonylphenol, NP; No observed effect level, NOEL; Organisation for Economic Cooperation and Development, OECD; ovariectomized, OVX.; postnatal day, pnd; Validation Management Group, VMG.

Acknowledgments

We acknowledge the dedicated efforts and work of the participating labs in generating these data, namely the Chemical Evaluation and Research Institute, Japan; the Food Drug Safety Centre, Japan; the Institute of Environmental Toxicology, Japan; Mitsubishi Chemical Safety Institute, Japan; Japan Bioassay Research Centre, Japan; Sumitomo Chemical Company, Japan; Syngenta Toxicology Laboratory, UK; TNO, the Netherlands; WIL Research Laboratories, USA; BASF, Germany; BAYER-AG, Germany; CIT, France; Aventis Crop Science, France; Exxon Biomedical Sciences Inc., USA; National Institute of Toxicological Research, Korea; Research Toxicology Center, Italy; and Institute of Biomedical Research, Italy. The acquisition of the chemical substances and the chemical repository for this validation program were sponsored by the European Chemical Industry Council (CEFIC) and the Japanese Chemical Industry Association (JCIA). Nonylphenol was kindly donated by Schenectady International Inc., and Bisphenol A was kindly donated by BAYER AG. We thank Joe Haseman for guidance and assistance with the design and conduct of statistical analysis and both Errol Zeiger and Herman Koëter for reviewing the manuscript.

Abstract:

The Organisation for Economic Co-operation and Development has completed Phase 2 of an international validation program for the rodent uterotrophic bioassay. The purpose of the validation program was to demonstrate the performance of two versions of the uterotrophic bioassay, the immature female rat and the adult ovariectomized rat, in four standardized protocols. This paper reports the dose response studies of the validation program, and the coded single dose studies are reported in an accompanying paper. The dose response study design used five selected weak estrogen agonists, bisphenol A, genistein, methoxychlor, nonylphenol, and *o,p'*-DDT. These weak agonists were administered in a prescribed series of doses in order to measure the performance and reproducibility of the protocols among the participating laboratories. All protocols successfully detected increases in uterine weights when the weak agonists were administered. Within each protocol, there was good agreement and reproducibility of the dose response among laboratories with each substance. Substance-specific variations were observed in the influence of the route of administration on the uterine response, the potency as related to the dose producing the first statistically significant increase in uterine weights, and the maximum increase in uterine weight. Substantive performance differences were not observed between the uterotrophic bioassay versions or among the standardized protocols, and these were judged to be qualitatively equivalent. It is noteworthy that these results were reproducible under a variety of different experimental conditions (e.g., animal strain, diet, housing, bedding, vehicle, animal age, and so on), indicating that the bioassay's performance as a screen is robust. In conclusion, both the intact, immature and the adult OVX versions and all protocols appear reproducible and transferable across laboratories and are able to detect weak estrogen agonists.